Phasic aortic flow velocity in patients with pulsus alternans[1]

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Phasic aortic flow velocity was recorded in two patients with pulsus alternans using a flow velocity probe connected to a Doppler ultrasonic flowmeter system. The variations in beat-to-beat peak velocity paralleled the variations in arterial and ventricular systolic pressures. This study provides direct evidence that stroke volume varies during this abnormal haemodynamic status. It is conceivable, though not proved in this study, that this phenomenon may be secondary to alternation between large and small end-diastolic fibre length.

Pulsus alternans is a physical sign observed in patients with borderline ventricular function curves or in patients with heart failure (Harris *et al.*, 1966; Ryan *et al.*, 1956; Fort *et al.*, 1969; Sancetta, 1955; Windle, 1917; De Rabago, Kohout, and Katz, 1955). The alternation of higher and lower peak systolic arterial or ventricular pressure is the characteristic finding in this condition despite the presence of regular rhythm. These variations in pressure are independent of the phases of respiration. This condition has been described in patients with hypertension, coronary artery disease, acquired aortic stenosis (Cooper, Braunwald, and Morrow, 1958), primary myocardial disease (Harris *et al.*, 1966), and in others (Cecil and Loeb, 1959; Green, 1960). Therefore, its presence is of pathological significance; however, in patients with heart disease it usually accompanies or precedes the onset of heart failure (Benchimol *et al.*, 1969). The mechanism responsible for the pulsus alternans is not completely understood, particularly because of lack of technique to measure phasic flow continuously.

The present investigation reports direct measurements of instantaneous phasic aortic flow velocity in two patients with pulsus alternans.

Case reports

Case 1 This was the first admission to this Institution for a 19-year-old white man who was in good health until August 1968, when he

was admitted to hospital because of fever and shortness of breath; he was diagnosed as having 'pneumonia'. Since then, he had progressive dyspnoea on effort, orthopnoea, peripheral oedema, cough, and weight gain. In February 1969, because of the persistence of these symptoms, he was digitalized and given diuretics. He lost 28·6 kg. in 9 days and experienced considerable symptomatic improvement.

Physical examination

Obese, his weight was 106 kg., height 183 cm., blood pressure 120/80 mm. Hg in both arms; pulse 90 a minute with occasional alternans. There was no cyanosis, clubbing of the fingers, or peripheral oedema. The jugular veins were slightly distended. The examination of the heart revealed the apex beat located in the fifth intercostal space to the left of the mid-clavicular line. The praecordium was hyperactive with a sustained left ventricular impulse; there were no thrills. On auscultation, the first heart sound was single and of a normal intensity. The second heart sound was physiologically split and the pulmonary component was accentuated. A fourth heart sound was heard at the mitral area. There were no murmurs. The liver and the spleen were not palpable. The lungs were clear to auscultation.

A phonocardiogram recorded with the apex cardiogram is shown in Fig. 1. The electrocardiogram and vectorcardiogram revealed left ventricular hypertrophy and strain (Fig. 2). The chest x-ray showed a globular heart shadow suggestive of a minimal degree of left ventricular enlargement (Fig. 3).

Cardiac catheterization on 15 May 1969 supported the diagnosis of primary myocardial disease of non-obstructive nature (Table). Cineangiograms showed no evidence of mitral valve insufficiency.
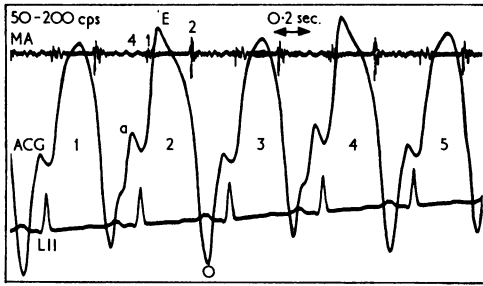
The patient was subsequently discharged on a

FIG. I *Phonocardiogram at the mitral area (MA) recorded in the range of 50 to 200 cycles/second, apex cardiogram (ACG), and lead II of the electrocardiogram in Case 1. Note pulsus alternans in the apex cardiogram. Beats 1, 3, and 5 have small amplitude of the systolic and 'a' waves as compared with beats 2 and 4. The phonocardiogram shows a fourth heart sound.*

programme of digitalis and diuretics, and further encouraged to continue to lose weight.

Case 2 A 32-year-old white man was admitted for evaluation of cardiomegaly. His past medical history was essentially negative except for severe bronchial asthma of 20 to 25 years' duration. In August 1968 he was admitted to hospital and was found to have cardiomegaly on the chest x-ray. Past examinations several years ago, including Army physical and insurance examinations, did not reveal cardiomegaly. At the present time, the patient complained of increasing dyspnoea on effort and considerable lethargy.

Physical examination

Blood pressure 110/80 mm. Hg in both arms, pulse 120 and regular; respiration 28 a minute and laboured. There was obvious distension of the neck veins. Auscultation of the lungs revealed rhonchi and inspiratory moist râles at both bases. The apex beat was located in the sixth intercostal space in the anterior axillary line, and had a sustained quality. Auscultation of the heart revealed a quadruple rhythm, due to loud third and fourth heart sounds. There was a grade 3/6, high frequency systolic regurgitant murmur at the mitral and tricuspid areas. A phonocardiogram confirmed the auscultatory findings. All peripheral pulses were present and showed pulsus alternans. Examination of the abdomen showed the liver to be 4 cm. below the right costal margin. Musculoskeletal system showed no abnormality and the neurological examination was normal.

The electrocardiogram and vectorcardiogram showed incomplete left bundle-branch block, low voltage in the limb leads, and abnormal T waves and ST segments (Fig. 4). The chest x-ray showed obvious cardiomegaly with predominant left ventricular enlargement, pulmonary congestion as well as changes consistent with early pulmonary emphysema (Fig. 5). Fluoroscopy on
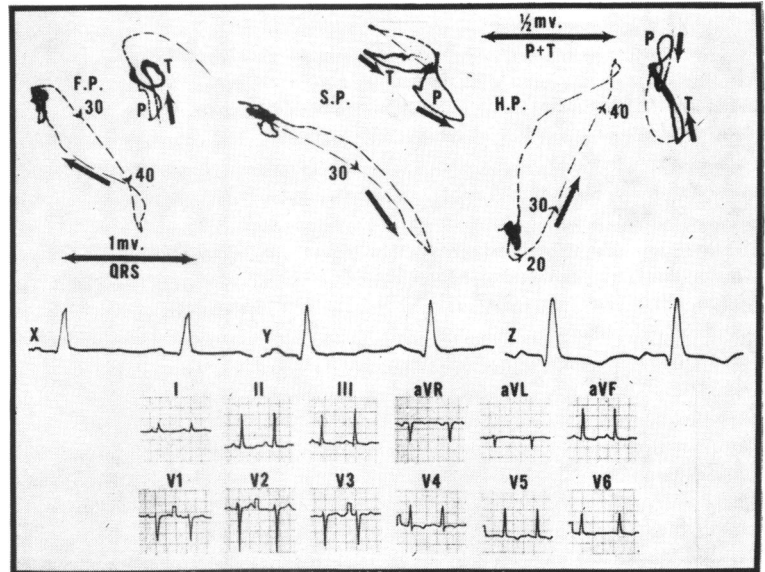

FIG. 2 *Vectorcardiogram recorded with a Frank system, X, Y, and Z leads, and electrocardiogram of Case 1. The rotation of the QRS loop is indicated by an arrow. The praecordial leads of the electrocardiogram were taken at half standard. Both electrocardiogram and vectorcardiogram show signs of left ventricular hypertrophy and strain.*

FIG. 3 *Chest x-ray of Case 1 showing a globular heart and suggestive evidence for left ventricular enlargement.*
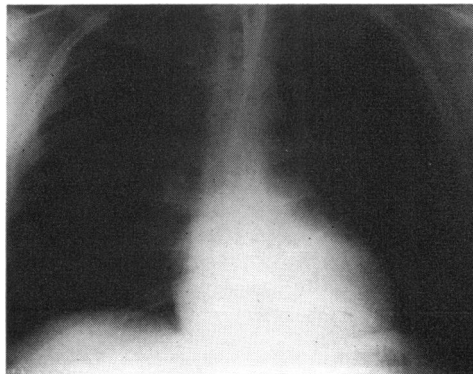
admission showed no evidence for pericardial effusion. The patient underwent cardiac catheterization and the findings supported the diagnosis of non-obstructive cardiomyopathy with mitral and tricuspid insufficiency (Table).

Methods of haemodynamic and flow velocity studies

Right and left heart catheterization were performed using standard techniques. The patients were non-sedated and post-absorptive. The

brachial artery and the medial antecubital vein were exposed under local anaesthesia (1% Carbocaine – Winthrop Laboratories) in the right antecubital fossa. A No. 7 end-lumen catheter was introduced into the vein and advanced to the right heart. Another end-lumen catheter was introduced into the brachial artery and advanced to the ascending aorta and left ventricle. Pressures were obtained with a Statham P23 Db strain gauge. The zero reference used for position of the transducer was the mid-point between the anterior and the posterior surface of the chest. Cardiac output was measured with indicator dilution technique using indocyanine-cardiogreen (Westcott-Dunning Laboratories) as the indicator; 3·1 mg. indicator were injected into the pulmonary artery, with sampling from the left ventricle or ascending aorta at a constant rate of 38·2 ml. per minute.

Right atrial, right ventricular, and aortic flow velocities were measured with the Doppler catheter (supplied by Southwest Research Institute, San Antonio, Texas) as developed by Stegall *et al.* (1967). The catheter was inserted at an arm vein and advanced to the right heart for the purpose of obtaining right atrial and right ventricular flow velocities. The catheter was connected to a Doppler ultrasonic flowmeter telemetry system (Franklin, Schlegel, and Rushmer, 1961; Franklin, Schlegel, and Watson, 1963). Simultaneous recordings of pressures, flow velocity, lead II of the electrocardiogram, and a phonocardiogram were made. The flowmeter audio signal, the analogue flow velocity records, intracardiac pressures, phonocardiograms, and electrocardiograms were recorded in a multi-channel oscillographic recorder (Electronics for Medicine, Model DR-12) at various paper speeds and on a multi-channel Sanborn tape recorder.

Results

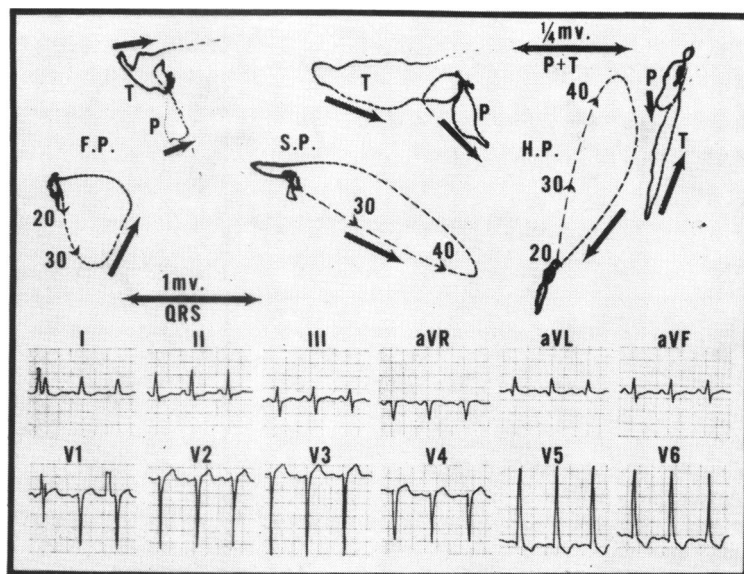There was no electrical alternans in these two cases and both had regular sinus rhythm.

FIG. 4   *Vectorcardiogram and electrocardiogram of Case 2 showing signs of left ventricular hypertrophy and strain.*

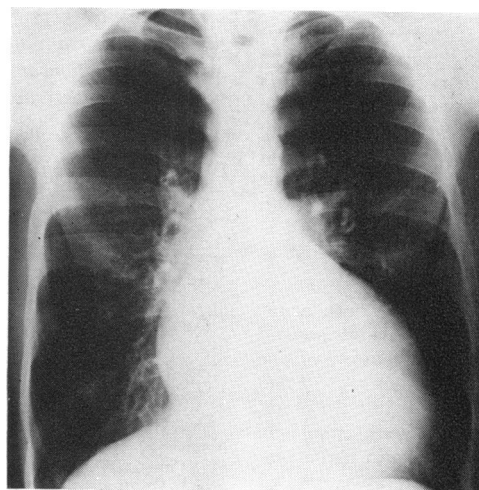FIG. 5   *Chest x-ray of Case 2 showing moderate degree of cardiomegaly and pulmonary congestion.*

TABLE   *Clinical and haemodynamic data*

Case No.	Age and sex	Grade	Electrocardiogram	X-ray	Pressures (mm. Hg)						Cardiac index (l./min./ m.²)	Heart rate (beats/ min.)	Stroke index (ml./beat/ m.²)	Peripheral resist. (dynes/ sec./ cm.⁻⁵)	Pulmon. resist. (dynes/ sec./ cm.⁻⁵)
					RA mean	RV S/D	PA S/D/M	Pulm. wedge mean	LV S/EDP	Aorta S/D/M					
1	19 M	2	Sinus rhythm LV hypertrophy strain	LV enlargement	10	60/10	60/20/40	30	130/31	130/80/100	3·0	108	27	1100	400
2	31 M	3	Sinus rhythm, incomplete LBBB, LV hypertrophy, strain	LV enlargement	3	38/6	38/22/20	—	116/30	116/78/92	1·5	105	15	2720	592

EDP=end-diastolic pressure; LBBB=left bundle-branch block.

Pulsus alternans was intermittently present in both cases. Measurements of pressure and flow velocity were made during periods of pulsus alternans.

Both cases had clinical evidence of heart failure at the time of the study. The electrocardiogram and vectorcardiogram showed abnormalities indicating left ventricular hypertrophy.

Case 2 had conspicuous cardiomegaly on the chest x-ray, and in Case 1 the heart size was at the upper limit of normal. The haemodynamic data of Case 1 revealed a moderate degree of pulmonary hypertension, increased pulmonary 'wedge' and left ventricular end-diastolic pressures, and normal cardiac output. The cine-angiograms showed no evidence of valvular insufficiency. Case 2 had only a slight increase in mean pulmonary artery pressure, but the left ventricular end-diastolic pressure was much increased; cardiac output was below the limits of normal. The cine-angiogram revealed obvious dyskinesia of the left ventricle with large left ventricular end-systolic and end-diastolic diameters. There was also evidence of moderate mitral insufficiency which was interpreted as secondary to left ventricular dilatation. Both cases had intermittent pulsus alternans on the left ventricular, right ventricular, aortic, and pulmonary artery pressure curves.

The magnitude of the pulsus alternans as measured by the difference in systolic pressures between the small and large beats varied between 10 and 30 mm. Hg. The variations in peak aortic flow velocity were accompanied by only 5 to 10 per cent variations in peak ventricular systolic pressures, as shown in Fig. 6, 7, and 8. The beats with smaller peak flow velocity had shorter ejection time, and lower peak ventricular, aortic, and pulmonary artery systolic pressures. The cardiac cycle in both cases during the periods of pulsus alternans was essentially identical.

Discussion

Most observations dealing with pulsus alternans have been made in experimental animals, and may not be directly applicable to man. The studies made in man are few in number and most of them deal primarily with the clinical significance of this finding or with the descriptions of variations in the direct or indirect pressure measurements or heart sounds (Fort *et al.*, 1969). Measurement of ventricular volume, however, has been obtained by Gleason and Braunwald (1962), using the technique of biplane cine-angiography and has elucidated some of the mechanisms of this condition. To our knowledge, there have
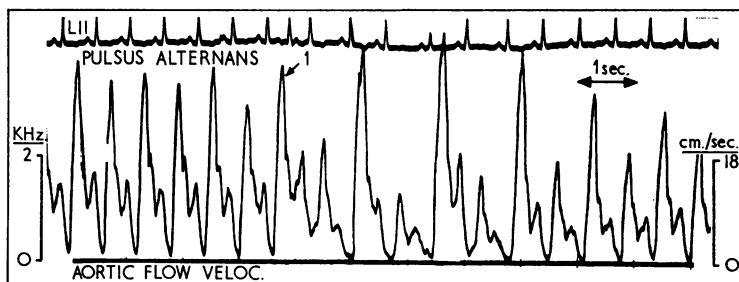
FIG. 6 *(Case 2) Lead II of the electrocardiogram and aortic flow velocity. A beat which followed an atrial extrasystole (first beat after the sinus beat marked '1') triggered the pulsus alternans.*

FIG. 7 *(Case 2) Aortic flow velocity and lead II of the electrocardiogram; note the variations in peak aortic flow velocity curves characteristic of pulsus alternans. KHz. = 9cm./sec. flow velocity.*
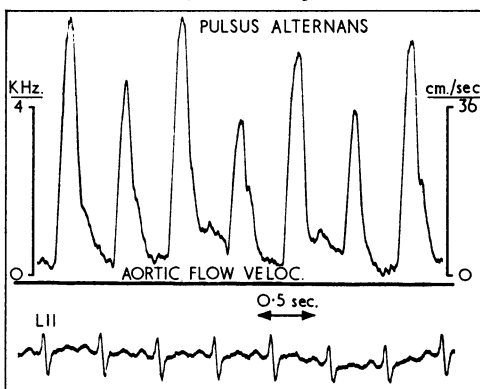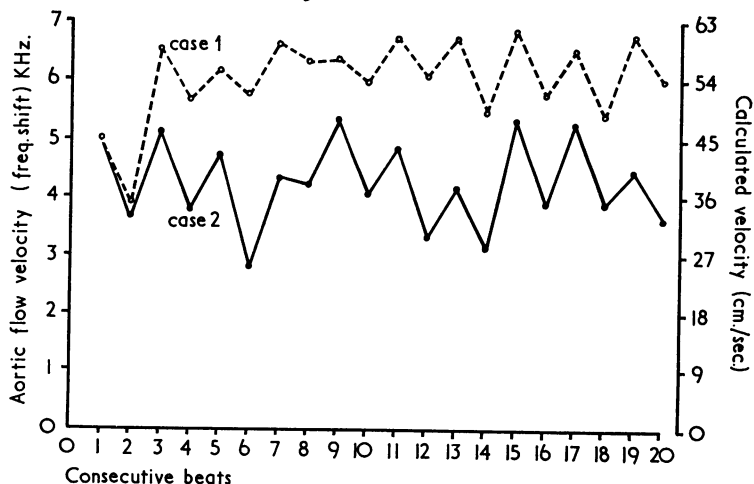
FIG. 8 *Measurement of peak flow velocity obtained in 20 consecutive beats in the two patients with pulsus alternans. KHz. = 9cm./sec. flow velocity.*

been no reports of direct measurement of instantaneous phasic aortic flow velocity in this condition.

The two basic physiological mechanisms which have been invoked to explain the presence of pulsus alternans are the alternate deletion of a number of contractile units (Wiggers, 1952) and the alternation of the end-diastolic fibre length with consequent alternation of the strength of contraction (Mitchell, Sonnenblick, and Sarnoff, 1961).

Gleason and Braunwald (1962) showed that the probable mechanism for the appearance of the pulsus alternans was the alternation between large and small end-diastolic fibre length. This, in turn, would result in more effective emptying of the ventricle with beats having large peak pressures accompanied by a more complete emptying of the ventricle; those beats associated with small pressures were accompanied by small stroke volume and an incomplete emptying of the ventricle. Our data provided direct evidence for the fact that aortic flow velocity, and thus stroke volume, alternated in the manner described by Gleason and Braunwald (1962). The beats accompanied by high peak arterial or ventricular pressures were invariably associated with a high peak aortic flow velocity, as shown in Fig. 6 and 7. Of interest was the fact that in one patient (Case 1) the pulsus alternans was, in fact, triggered by the presence of an extrasystole (Fig. 6). It appeared that the long diastolic filling period which followed the extrasystole resulted in a large ventricular end-diastolic volume which initiated the cycle of flow and pressure alternans. Others have also reported that pulsus alternans may be precipitated by erect posture, phlebotomy, or venous pooling, and diminished by recumbency, exercise, transfusion, and other factors increasing venous return (Mitchell *et al.*, 1961).

In connexion with this study, it is pertinent to state that pulsus alternans may occur in normal subjects in the absence of any form of heart disease, as has been described by others in the past. Our previously reported observations (Benchimol *et al.*, 1969) indicate that, when the right ventricle or the right atrium were paced at a rapid heart rate, pulsus alternans could occur, particularly at pacing rates above 140/min. (Fig. 8).

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